

**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
Washington, D.C. 20549  
FORM 8-K**

**CURRENT REPORT  
Pursuant to Section 13 OR 15(d) of The Securities Exchange Act of 1934**

**Date of Report (date of earliest event reported): August 9, 2022**

**Neoleukin Therapeutics, Inc.**

(Exact name of registrant as specified in its charter)

**Delaware**  
(State or other jurisdiction of incorporation or organization)

**001-36327**  
(Commission File Number)

**98-0542593**  
(I.R.S. Employer Identification No.)

**188 East Blaine Street, Suite 450**  
**Seattle, Washington 98102**  
(Address of principal executive offices) (Zip Code)  
Registrant's telephone number, including area code (866) 245-0312

N/A  
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, \$0.000001 par value	NLTX	The Nasdaq Global Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. Emerging growth company

**Item 2.02 Results of Operations and Financial Condition**

On August 9, 2022, Neoleukin Therapeutics, Inc. (the “Company”) issued a press release announcing financial results for the quarter ended June 30, 2022. The full text of the press release announcing such results is attached as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference.

**Item 7.01 Regulation FD Disclosure**

The Company has prepared investor presentation materials with information about the Company, which it intends to use as part of investor presentations. A copy of the investor presentation materials to be used by management for presentations is attached as Exhibit 99.2 to this Current Report on Form 8-K and is incorporated herein by reference.

The information in this current report on Form 8-K and in Exhibits 99.1 and 99.2 attached hereto is being furnished, but shall not be deemed “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (“Exchange Act”), and is not incorporated by reference into any filing of the Company under the Securities Act of 1933, as amended, or the Exchange Act, whether made before or after the date hereof, regardless of any general incorporation language in such filing.

**Item 9.01 Financial Statements and Exhibits**

(d) Exhibits

<u>Number</u>	<u>Description</u>
99.1	<a href="#">Press Release of Neoleukin Therapeutics, Inc. dated August 9, 2022</a>
99.2	<a href="#">Presentation of Neoleukin Therapeutics, Inc. dated August 2022</a>
104	Cover Page Interactive Data File (formatted as Inline XBRL)

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**SIGNATURE**

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

Date: August 9, 2022

**Neoleukin Therapeutics, Inc.**

By: /s/ Jonathan G. Drachman

Name: Jonathan G. Drachman

Title: President and Chief Executive Officer



## Neoleukin Therapeutics Announces Second Quarter 2022 Financial Results & Provides Corporate Update

– Company to Host Conference Call Today, August 9, 2022, at 1:30 p.m. Pacific / 4:30 p.m. Eastern -

**SEATTLE, Washington, August 9, 2022** – Neoleukin Therapeutics, Inc., “Neoleukin” (NASDAQ:NLTX), a biopharmaceutical company utilizing sophisticated computational methods to design *de novo* protein therapeutics, today announced financial results for the second quarter ended June 30, 2022 and a midyear corporate update.

“Our focus at Neoleukin is the advancement of *de novo* proteins to solve important therapeutic challenges and address unmet medical needs,” said Jonathan Drachman, M.D., Chief Executive Officer of Neoleukin. “We are excited to be part of a revolutionary approach to creating therapeutic proteins that are not based on native sequences. Our first programs, including our lead product candidate, NL-201, were developed using sophisticated computational algorithms combined with directed evolution in the laboratory. We have now added machine learning and neural networks to our technological approach, enabling faster, more accurate development of increasingly complex proteins. Using these new processes, we have been able to add two new cytokine mimetics to our discovery pipeline this year.”

“At Neoleukin, we are excited to be testing NL-201, which we believe is the first fully *de novo* protein in clinical trials,” said Priti Patel, M.D., Chief Medical Officer. “We are pleased to have begun testing NL-201 in combination with pembrolizumab in mid-May of this year. We believe this is just one of many potential opportunities to harness the immune activating properties of NL-201 in novel combination regimens.”

### NL-201 Update

Neoleukin is conducting a clinical trial of intravenous NL-201 in patients with advanced solid tumors. The trial is evaluating two different schedules and multiple dose levels in order to determine a recommended Phase 2 dose and schedule. Intermediate dose levels have been added to both schedules, which has extended the timeline to reach the anticipated Phase 2 dose. Dose escalation continues in both schedules, and Neoleukin now anticipates disclosing interim data in 2023.

In April 2022, Neoleukin announced the presentation of preclinical data at the American Association for Cancer Research (AACR) Annual Meeting, highlighting the potential for NL-201 to treat non-Hodgkin lymphoma as well as synergistic antitumor activity when NL-201 is combined with radiation therapy, including significant inhibition of tumor growth and increased survival in preclinical models.

In May 2022, Neoleukin announced treatment of the first patient in a combination arm evaluating the safety and efficacy of Neoleukin's NL-201 in combination with Merck's anti-PD-1 therapy KEYTRUDA® (pembrolizumab), as part of Neoleukin's ongoing Phase 1 trial. Up to 132 patients will be enrolled in the combination arm of the study, which is being conducted through a clinical collaboration and supply agreement with Merck (known as MSD outside the United States and Canada). The trial is assessing safety, pharmacokinetics, pharmacodynamics, immunogenicity, and antitumor activity. KEYTRUDA® is a registered trademark of Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

### Research Updates

**Technology:** Neoleukin's research team is actively engaged in the discovery of additional *de novo* cytokine mimetics as well as technological advances in order to accelerate the process from concept to proof of preclinical activity. Among these advances, the use of machine learning and neural networks have made it possible to design *de novo* proteins even when high-resolution structures have not yet been solved, using less compute resources and with a higher percentage of functional sequences. In addition to NL-201, Neoleukin has previously reported preclinical data for two *de novo* proteins: NL-CVX1, a decoy protein that mimics the human ACE2 binding site of the SARs-CoV2 spike protein and Neo-5171, an inhibitor of both IL-2 and IL-15 signaling.

**Pipeline:** Neoleukin is exploring an activator of T-regulatory cells for the treatment of inflammation and autoimmune diseases, a next generation IL-2/IL-15 agonist, and two additional undisclosed *de novo* cytokine mimetics for the treatment of cancer.

### Summary of Financial Results

**Cash Position:** Cash, cash equivalents, and short-term investments totaled \$116.5 million as of June 30, 2022, compared to \$142.5 million as of December 31, 2021.

Based upon current internal infrastructure and pipeline initiatives, Neoleukin believes it has sufficient cash to fund operations through 2023.

**R&D Expenses:** Research and development expenses for the second quarter of 2022 increased to \$11.0 million from \$9.8 million for the second quarter of 2021. The increase was primarily due to increased clinical trial expenses related to NL-201.

**G&A Expenses:** General and administrative expenses for the second quarter of 2022 decreased to \$4.9 million from \$5.3 million for the second quarter of 2021. The decrease was primarily attributable to decreases in personnel-related and facility-related costs.

**Net Loss:** Net loss for the second quarter of 2022 was \$15.7 million compared to a net loss of \$15.1 million in the second quarter of 2021.

### About NL-201

NL-201 is a *de novo* agonist of the IL-2 and IL-15 receptors, designed to expand cancer-fighting CD8 T cells and natural killer (NK) cells without any bias toward cells expressing the alpha receptor subunit (CD25). Previously presented preclinical data has demonstrated the ability of NL-201 to stimulate and expand CD8+ and NK cells at low doses with minimal impact on immunosuppressive regulatory T cells. Furthermore, NL-201 has demonstrated both monotherapy and combination activity across a wide range of preclinical syngeneic tumor models.

**Conference Call Information**

Neoleukin will host a conference call today to provide a second quarter corporate update and review financials. Details are as follows:

Date: August 9, 2022

Time: 1:30 p.m. Pacific / 4:30 p.m. Eastern

Toll-free: (800) 715-9871

Conference ID: 4116795

Webcast URL: <http://investor.neoleukin.com/events>

The archived audio webcast with slides will be available on the Investor Relations section of the Neoleukin website approximately two hours after the event and will be available for replay for at least 30 days after the event.

**About Neoleukin Therapeutics, Inc.**

Neoleukin is a biopharmaceutical company creating next generation immunotherapies for cancer, inflammation and autoimmunity using *de novo* protein design technology. Neoleukin uses sophisticated computational methods to design proteins that demonstrate specific pharmaceutical properties that provide potentially superior therapeutic benefit over native proteins. Neoleukin's lead product candidate, NL-201, is a combined IL-2 and IL-15 agonist designed to improve tolerability and activity by eliminating the alpha receptor binding interface. For more information, please visit the Neoleukin website: [www.neoleukin.com](http://www.neoleukin.com).

**Safe Harbor / Forward-Looking Statements**

This press release contains "forward-looking" statements within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995, including, but not limited to, statements regarding the therapeutic properties and potential of the company's *de novo* protein design technology, the results and timing of the clinical trial for NL-201, expectations regarding cash forecasts, and planned clinical and development activities and timelines. Forward-looking statements can be identified by words such as: "anticipate," "intend," "plan," "goal," "seek," "believe," "project," "estimate," "expect," "strategy," "future," "likely," "may," "should," "will" and similar references to future periods. These statements are subject to numerous risks and uncertainties, including risks and uncertainties related to the company's cash forecasts, the company's ability to advance its product candidates, the receipt and timing of potential regulatory submissions, designations, approvals and commercialization of product candidates, our ability to protect our intellectual property, the timing and results of preclinical and clinical trials, changes to laws or regulations, market conditions, geopolitical events, and further impacts of COVID-19, that could cause actual results to differ materially from what Neoleukin expects. Further information on potential risk factors that could affect Neoleukin's business and its financial results are detailed under the heading "Risk Factors" included in Neoleukin's Quarterly Reports on Form 10-Q and Annual Reports on Form 10-K filed from time to time with the Securities and Exchange Commission (SEC). Neoleukin undertakes no obligation to publicly update any forward-looking statement, whether written or oral, that may be made from time to time, whether as a result of new information, future developments or otherwise.

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Solebury Trout  
Alexandra Roy  
617-221-9197  
aroy@soleburytrout.com

**NEOLEUKIN THERAPEUTICS, INC.**  
**Condensed consolidated balance sheet data**  
(In thousands of U.S. dollars)

	June 30, 2022	December 31, 2021
<b>Assets</b>		
Cash, cash equivalents, and short-term investments	\$ 116,457	\$ 142,467
Other current assets	2,028	1,522
Non-current assets	18,536	19,274
<b>Total assets</b>	<b>\$ 137,021</b>	<b>\$ 163,263</b>
<b>Liabilities</b>		
Current liabilities	\$ 9,271	\$ 8,636
Non-current liabilities	11,042	11,763
Total liabilities	20,313	20,399
Stockholders' equity	116,708	142,864
<b>Total liabilities and stockholders' equity</b>	<b>\$ 137,021</b>	<b>\$ 163,263</b>

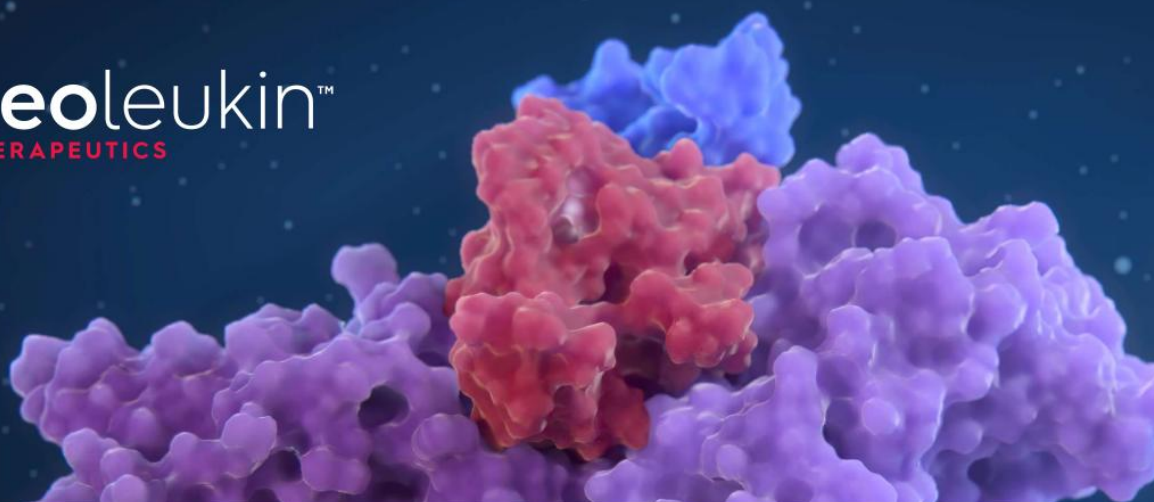


## NEOLEUKIN THERAPEUTICS, INC.

## Condensed consolidated statements of operations

(In thousands of U.S. dollars, except per share and share amounts)

	Three Months Ended June 30,		Six Months Ended June 30,	
	2022	2021	2022	2021
<b>Operating expenses</b>				
Research and development	\$ 10,956	\$ 9,824	\$ 21,656	\$ 19,506
General and administrative	4,915	5,300	9,580	10,566
<b>Total operating expenses</b>	15,871	15,124	31,236	30,072
Loss from operations	(15,871)	(15,124)	(31,236)	(30,072)
Other income (loss), net	183	(5)	197	(7)
<b>Net loss</b>	<u>\$ (15,688)</u>	<u>\$ (15,129)</u>	<u>\$ (31,039)</u>	<u>\$ (30,079)</u>
<b>Comprehensive income (loss):</b>				
Unrealized loss on available-for-sale securities	(72)	—	(72)	—
<b>Comprehensive loss</b>	<u>\$ (15,760)</u>	<u>\$ (15,129)</u>	<u>\$ (31,111)</u>	<u>\$ (30,079)</u>
Net loss per share – basic and diluted	\$ (0.28)	\$ (0.27)	\$ (0.56)	\$ (0.55)
Basic and diluted weighted average common shares outstanding	55,203,709	55,026,404	55,173,789	54,985,639



# Corporate Presentation

August 2022

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# Forward Looking Statements







Certain of the statements made in these slides and the accompanying oral presentation are forward looking, including those relating to Neoleukin's business, strategy, future operations, advancement of its product candidates and product pipeline, clinical development of its product candidates, including expectations regarding timing of regulatory submissions and initiation of clinical trials, regulatory requirements for initiation of clinical trials and registration of product candidates, properties of its product candidates, availability of data, the use and sufficiency of its cash resources, and other statements containing the words "anticipate," "believe," "expect," "may," "plan," "project," "potential," "will," "would," "could," "continue," and similar expressions. These statements are subject to risks and uncertainties that could cause actual results and events to differ materially from those anticipated, including, but not limited to, risks and uncertainties related to: whether results of early clinical trials or preclinical studies will be indicative of the results of future trials, the adequacy of any clinical models, uncertainties associated with regulatory review of clinical trials, its ability to identify or acquire additional clinical candidates, its ability to obtain and maintain regulatory approval for any product candidates and the potential safety, efficacy or clinical utility of or any product candidates; further impacts of COVID-19, supply chain disruptions, or other global economic and geopolitical events on its operations; and other factors discussed in the "Risk Factors" section and elsewhere in the Company's Quarterly Report on Form 10-Q for the quarter ended June 30, 2022, Annual Report on Form 10-K for the fiscal year ended December 31, 2021, and subsequent reports as filed with the Securities and Exchange Commission. Actual results or developments may differ materially from those projected or implied in these forward-looking statements. The Company disclaims any intention or obligation to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise.



We use protein design to reinvent how therapies are created with a goal to meaningfully improve patients' lives

Neoleukin is a pioneer in *de novo* protein development, leveraging computational methods to create new therapies. This new approach has unlimited potential to treat human disease by improving on nature, designing for life. We are building a company with a vibrant and inclusive culture that we believe will make a meaningful impact for patients, our people and our community.

# Neoleukin: Leader in *de novo* Protein Therapeutics

2018	2019	2020	2021	2022	FUTURE
 <p><b>NEOLEUKIN FOUNDED</b></p> <p>Computational methods enable fully <i>de novo</i> protein design</p> <p>Scientists and technology spun out of University of Washington</p>	 <p><b>MERGER COMPLETED</b></p> <p>NASDAQ listing (NLTX) after merger with Aquinox</p> <p>More than \$140M raised through merger and follow-on offering</p>	 <p><b>FIRST IND SUBMITTED</b></p> <p>First IND of fully <i>de novo</i> protein (NL-201)</p> <p>Neoleukin scientists create second fully <i>de novo</i> protein (NL-CVX1)</p>	 <p><b>PHASE 1 TRIAL INITIATED</b></p> <p>First patients treated with fully <i>de novo</i> protein</p> <p>Experienced drug-developers added in Clinical and Research</p>	 <p><b>MACHINE LEARNING</b></p> <p>Machine learning/neural network technology enables rapid drug discovery</p>	 <p><b>EXPAND <i>DE NOVO</i> PROTEIN PIPELINE</b></p> <p>Multiple fully <i>de novo</i> molecules expected to be developed in oncology and autoimmune disease</p> <p>Innovative approaches to drug delivery, conditional activation, and affinity optimization to improve therapeutic index</p>



# Leadership Team



**Jonathan Drachman, M.D.**

Chief Executive Officer

**PRIOR**  
CMO, EVP R&D  
Seagen



**Bill Arthur, Ph.D.**

VP & Head of Research

**PRIOR**  
Seagen  
Merck & Co.



**Priti Patel, M.D., M.P.H.**

Chief Medical Officer

**PRIOR**  
AstraZeneca  
Acerta Pharma



**Donna Cochener**

General Counsel, SVP Legal

**PRIOR**  
HomeStreet  
Davis Wright Tremain



**Carl Walkey, Ph.D.**

Senior VP, Corporate  
Development

**PRIOR**  
Postdoctoral Fellow,  
UW-IPD



**Sean Smith**

VP, Finance

**PRIOR**  
Aptevo Therapeutics  
KPMG

# Better Therapies by Design




Functional *de novo* proteins

nature

2019

Article | Published: 09 January 2019

## De novo design of potent and selective mimics of IL-2 and IL-15

Daniel-Adriano Silva , Shawn Yu, Umut Y. Ulge, Jamie B. Spangler, Kevin M. Jude, Carlos Labão-Almeida, Lestat R. Ali, Alfredo Quijano-Rubio, Mikel Ruterbusch, Isabel Leung, Tamara Biary, Stephanie J. Crowley, Enrique Marcos, Carl D. Walkey, Brian D. Weitzner, Fátima Pardo-Avila, Javier Castellanos, Lauren Carter, Lance Stewart, Stanley R. Riddell, Marion Pepper, Gonçalo J. L. Bernardes, Michael Dougan, K. Christopher Garcia  & David Baker 

Science  
AAAS

2020

CORONAVIRUS

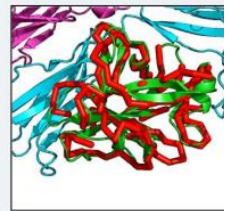
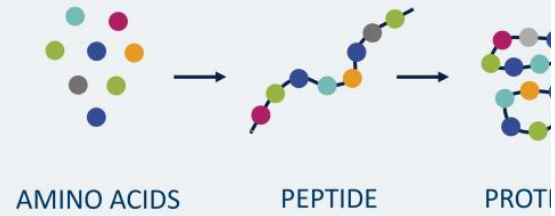
## De novo design of potent and resilient hACE2 decoys to neutralize SARS-CoV-2

Thomas W. Linsky<sup>1,6</sup>, Renan Vergara<sup>1,6</sup>, Nuria Codina<sup>1,6</sup>, Jorgen W. Nelson<sup>1,6</sup>, Matthew J. Walker<sup>1</sup>, Wen Su<sup>2</sup>, Christopher O. Barnes<sup>3</sup>, Tien-Ying Hsiang<sup>4</sup>, Katharina Esser-Nobis<sup>4</sup>, Kevin Yu<sup>1</sup>, Z. Beau Reneer<sup>5</sup>, Yixuan J. Hou<sup>4</sup>, Tanu Priya<sup>1</sup>, Masaya Mitsumoto<sup>1</sup>, Avery Pong<sup>1</sup>, Uland Y. Lau<sup>1</sup>, Marsha L. Mason<sup>1</sup>, Jerry Chen<sup>1</sup>, Alex Chen<sup>1</sup>, Tania Berrocal<sup>1</sup>, Hong Peng<sup>1</sup>, Nicole S. Clairmont<sup>1</sup>, Javier Castellanos<sup>1</sup>, Yu-Ru Lin<sup>1</sup>, Anna Josephson-Day<sup>1</sup>, Ralph S. Baric<sup>6</sup>, Deborah H. Fuller<sup>7</sup>, Carl D. Walkey<sup>1</sup>, Ted M. Ross<sup>5,8</sup>, Ryan Swanson<sup>1</sup>, Pamela J. Bjorkman<sup>9</sup>, Michael Gale Jr.<sup>4</sup>, Luis M. Blancas-Mejia<sup>1</sup>, Hui-Ling Yen<sup>2</sup>, Daniel-Adriano Silva<sup>1,†</sup>

- Scientific founders are world leaders in *de novo* protein design
- Technology originated at University of Washington Institute for Protein Design
- Exclusive license obtained for commercialization of NL-201 and other *de novo* protein assets

# De Novo Protein Design

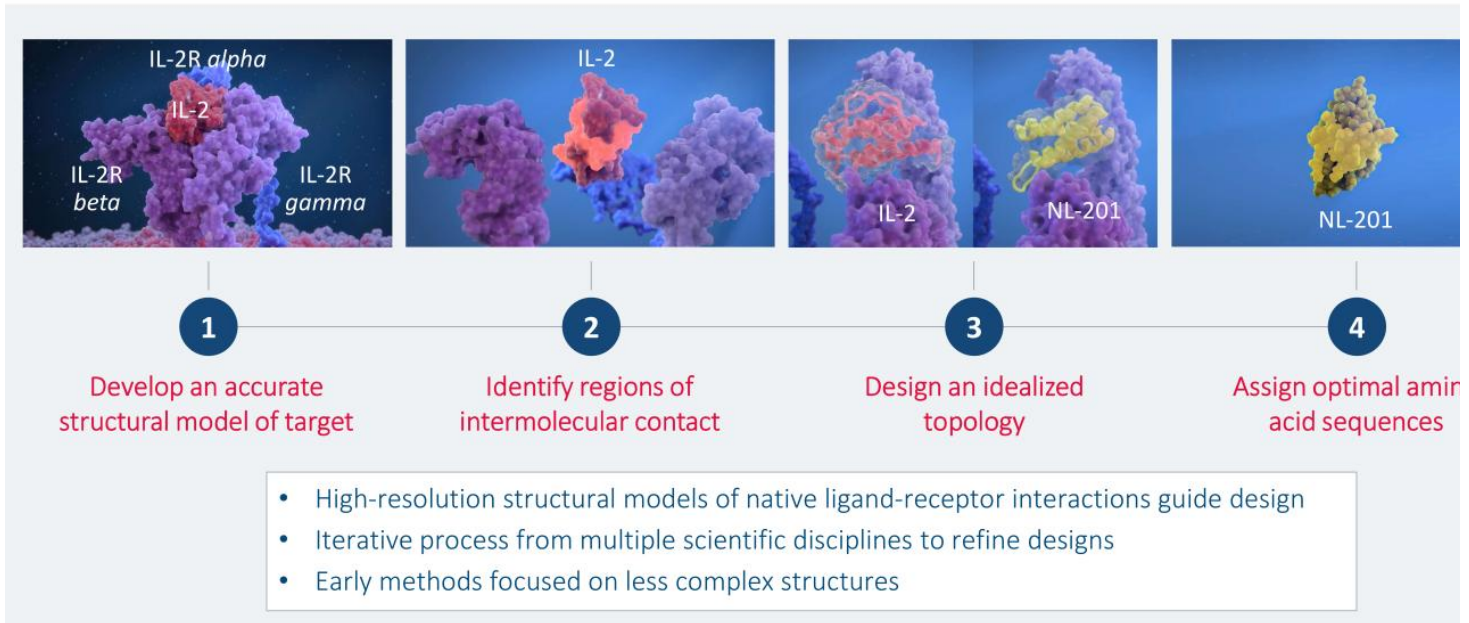
- Amino acids are nature's building blocks for proteins
- The order they are arranged in determines how a protein folds, what it binds to, and what it does
- Decades of research into protein folding, thermodynamics, and advances in computational power has resulted in the ability to design proteins that have never existed before



Neoleukin is leading the revolution in *de novo* protein therapeutics

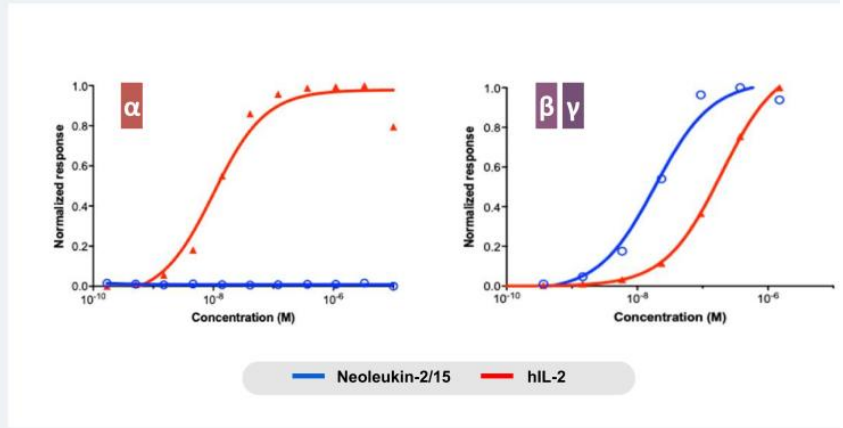
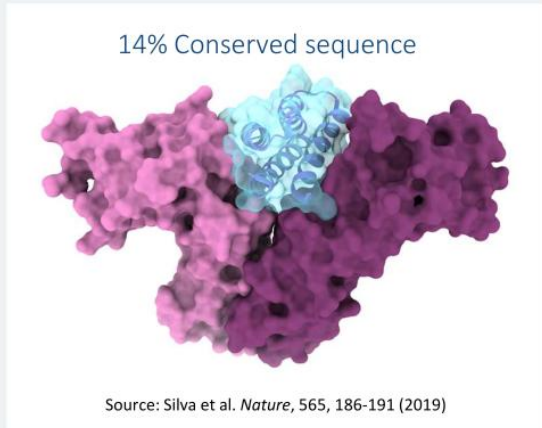


# Neoleukin™ *de novo* design methodology



# NL-201: *de novo* non-alpha IL-2/IL-15 agonist

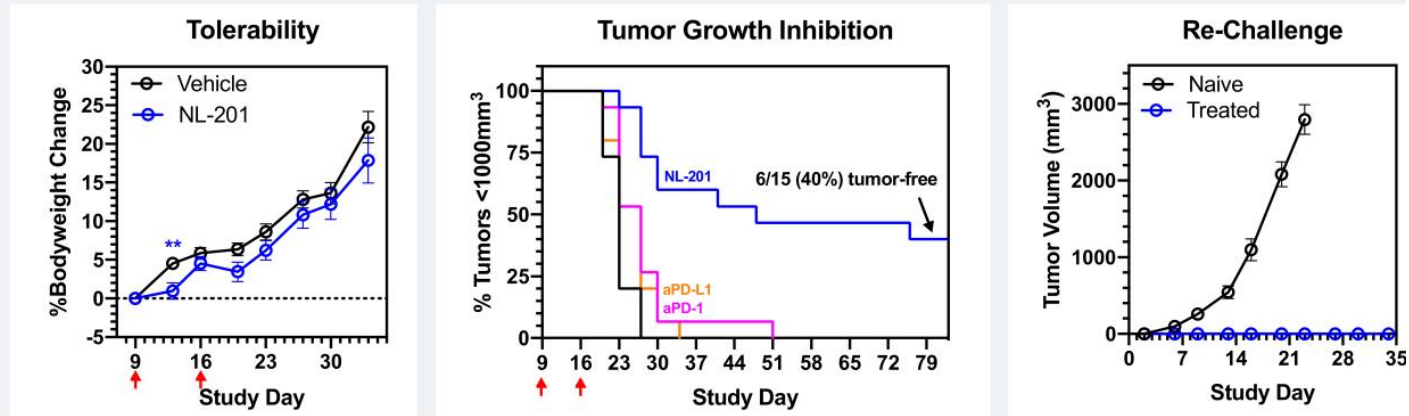
Potent, stable, no bias toward Tregs or endothelial cells



NL-201 is a *de novo* protein designed with no alpha subunit interaction and increased beta/gamma binding

# NL-201: Durable Antitumor Activity at Well-tolerated Doses

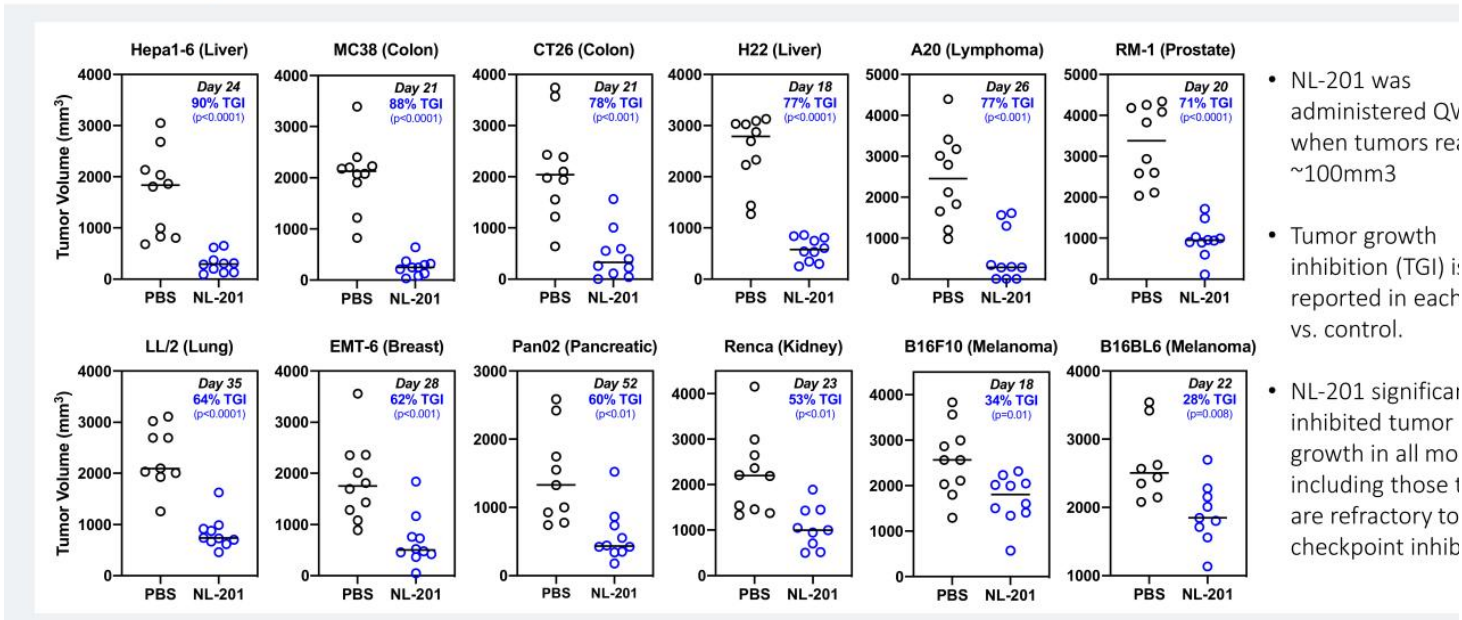
## CT26 syngeneic murine colon cancer model



- NL-201 is well-tolerated at therapeutic doses
- Single-agent activity observed
- Tumor-free mice reject CT26 upon re-challenge

Walkey et. al, AACR Virtual Annual Meeting II, Abstract #4518, June 2020

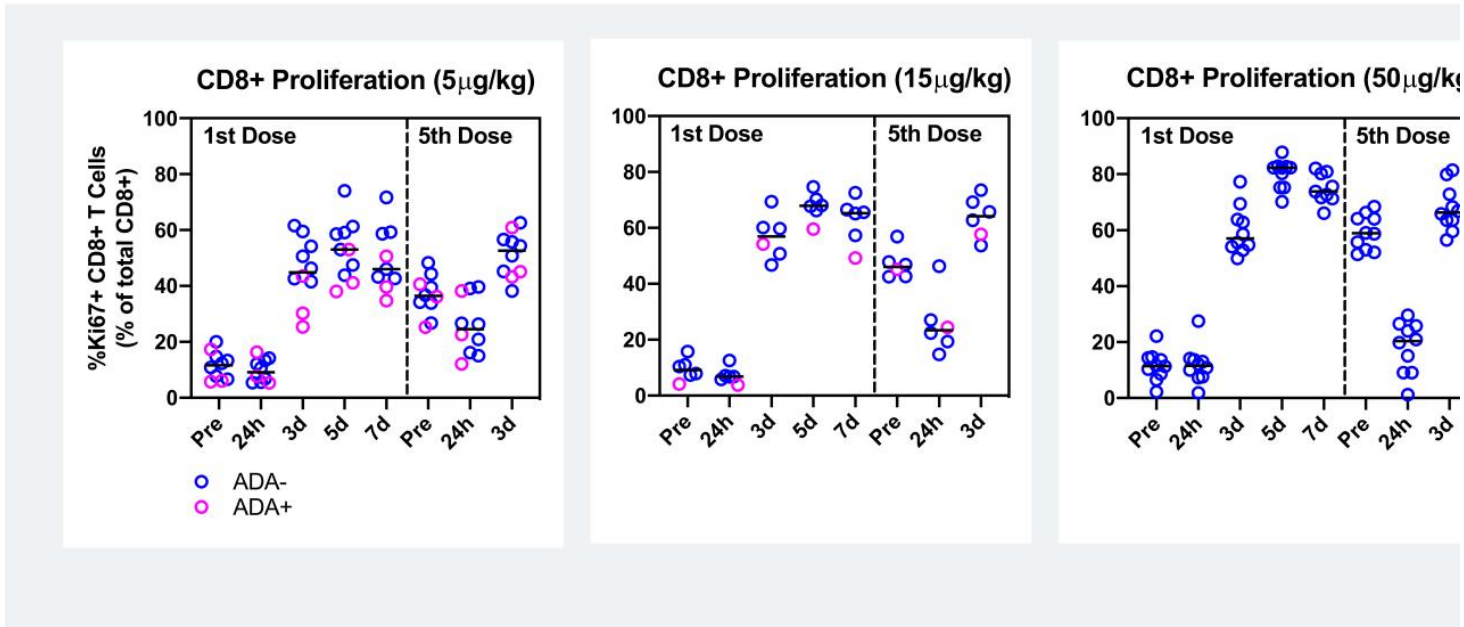
# NL-201 Demonstrates Robust Single-Agent Activity in Multiple Tumor Models



- NL-201 was administered Qw when tumors reached ~100mm<sup>3</sup>
- Tumor growth inhibition (TGI) is reported in each vs. control.
- NL-201 significantly inhibited tumor growth in all models, including those that are refractory to checkpoint inhibition.

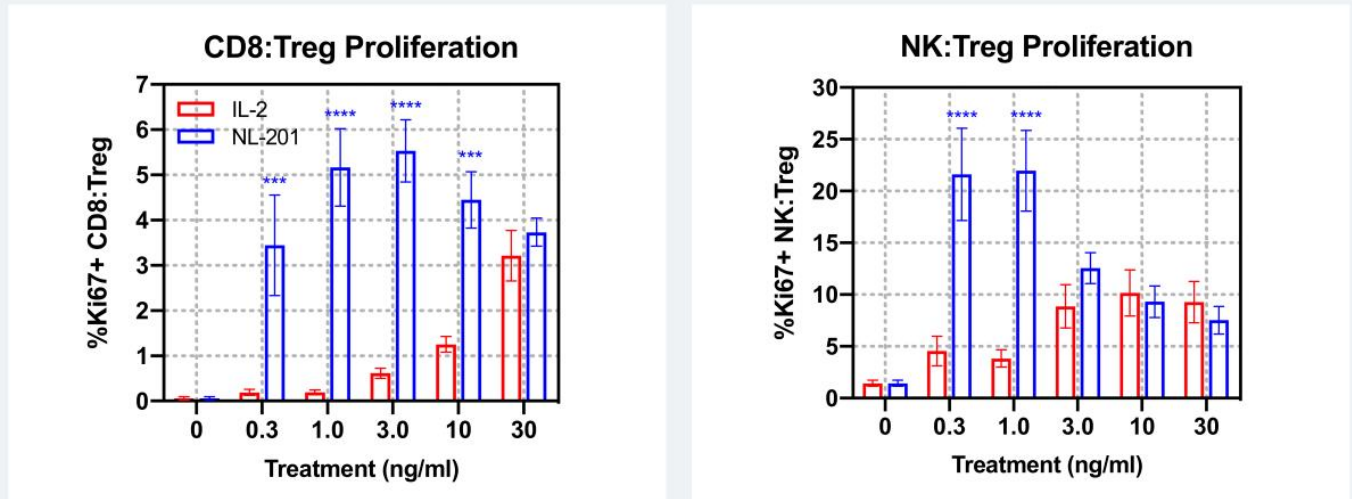
Walkey et. al, AACR Virtual Annual Meeting II, Abstract #4518, June 2020

# Similar Pharmacodynamic Response in ADA+ vs ADA- NH



Walkey et. al, AACR Virtual Annual Meeting II, Abstract #4518, June 2020

# NL-201: High CD8:Treg and NK:Treg Ratios at Low Concentration



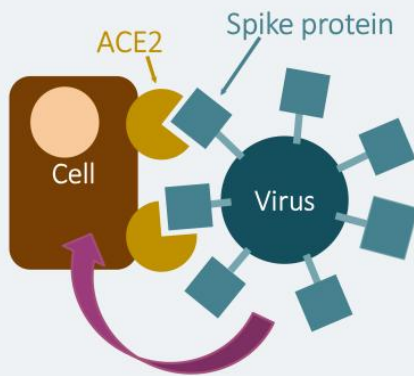
NL-201 vs IL-2: \* p<0.05; \*\* p<0.01; \*\*\* p<0.001; \*\*\*\* p<0.0001

Walkey et. al, AACR Virtual Annual Meeting II, Abstract #4518, June 2020



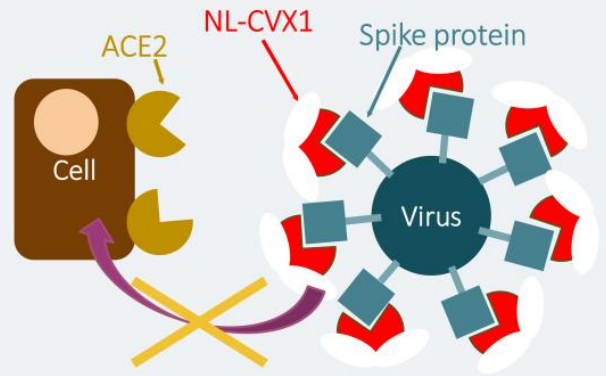
# De Novo Platform Potential: COVID-19

**SARS-CoV-2 uses ACE2 as a receptor to gain access to and infect cells**



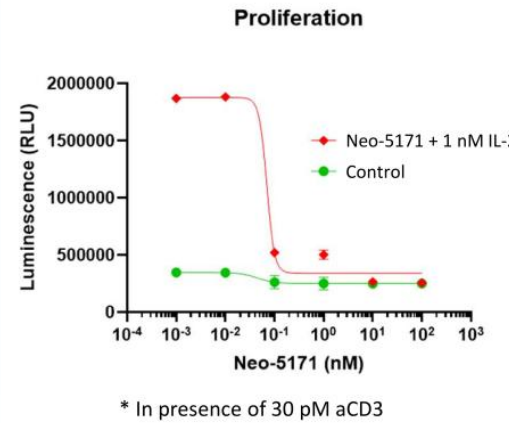
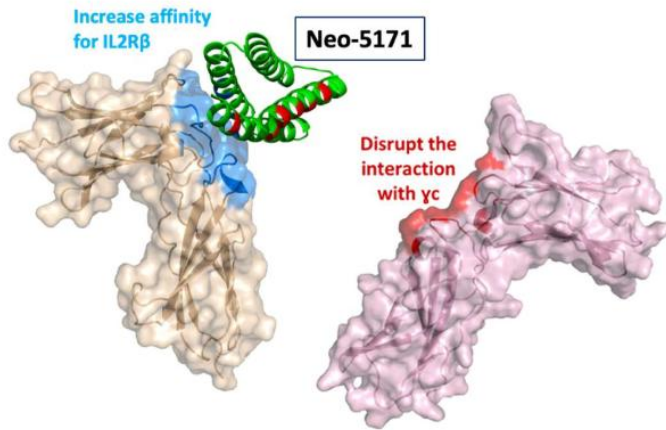
**NL-CVX1 - *de novo* ACE2 decoy:**

- *Binds to SARS-CoV2 spike protein*
- *Inhibits viral infection in vitro*



*De Novo* protein designed, tested, and optimized in the pre-clinical setting in ~10 weeks

# Neo-5171: A computationally designed *de novo* protein inhibitor of IL-2 and IL-15 signaling

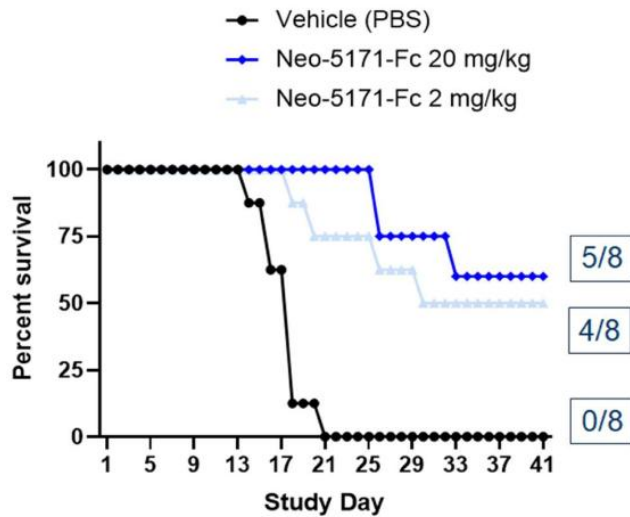


- Potent inhibitor of CD8 T-cell proliferation and IFN-g production
- Resistant to proteases and low pH
- Less impact on T-regulatory cells

R. Swanson et. al. Am. Coll Rheum. (ACR) 2021; Abstract 1438, Nov 2021



# Neo-5171-Fc prolongs survival in a preclinical model of graft-vs-host disease (GVHD)

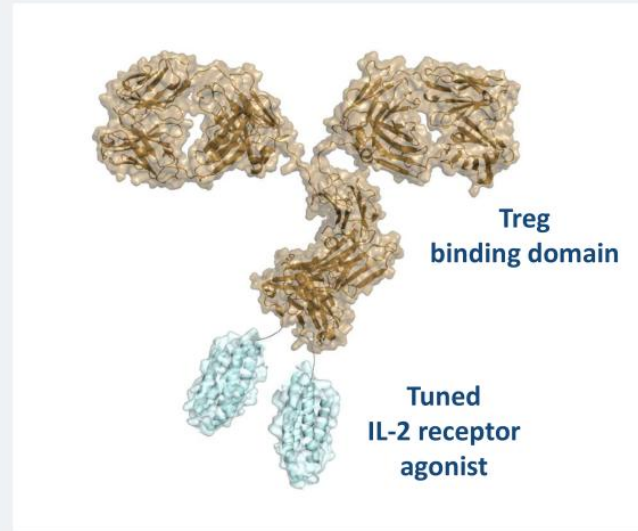


- Immunodeficient NSG mice were irradiated and received  $10^7$  human PBMC on Day -1
- Intraperitoneal dosing with Neo-5171-Fc q3d, beginning Day 0
- Mice were euthanized when experiencing >20% body weight loss
- At high dose 62.5% of mice survived at study end (Day 42)

R. Swanson et. al. Am. Coll Rheum. (ACR) 2021; Abstract 1438, Nov 2021

# Highly Selective *De Novo* Treg Expander and Activator

- Highly tuned CD122/CD132 activator fused to Treg-targeting domain
- Potential to specifically expand Tregs for the treatment of autoimmune diseases and inflammation
- Finely tuned *de novo* protein to achieve optimal affinity and potency for specificity and cis-activation
- Demonstrated ability to drive specificity by targeting *de novo* cytokine mimetics



# Evolution of Neoleukin™ *De Novo* Protein Technology

*Accelerating speed and accuracy*



- New methodology combines machine-learning (ML) based sequence design and structure prediction with high-throughput screening.
- ML-based methods enable more efficient protein design with higher success rates and using a fraction of the computational power.
- We can now develop from a more expanded landscape of protein topologies that were not accessible by traditional methods.

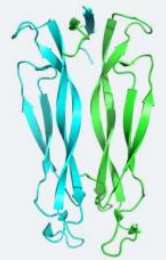
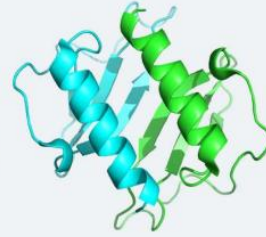
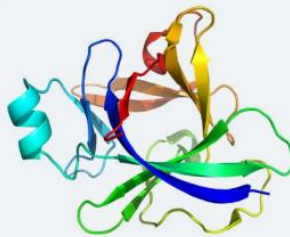
# Adding Machine Learning to Protein Design

*Building the next generation of de novo proteins*

New methods are required to tackle more complex topologies

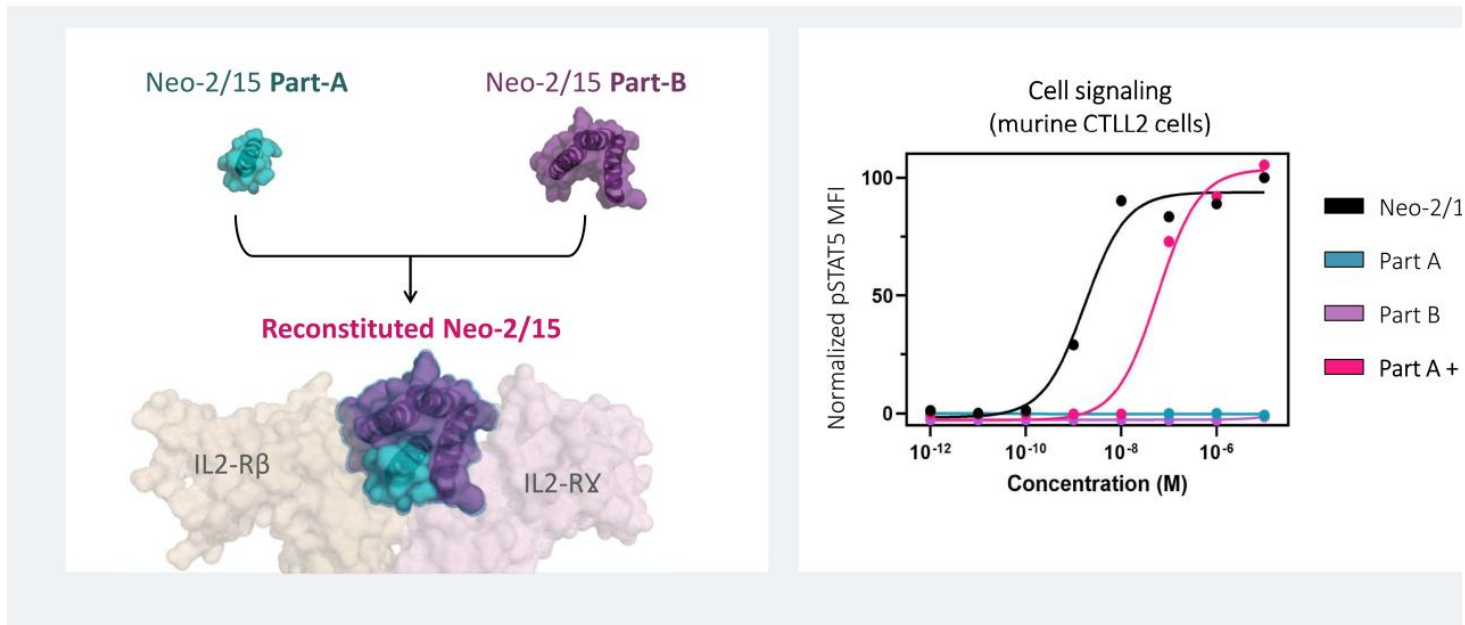


4-helix bundle



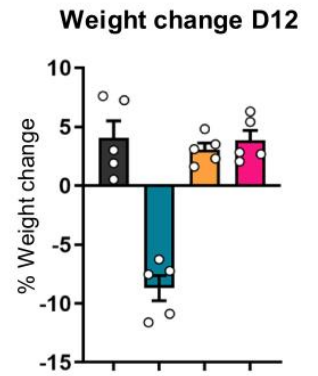
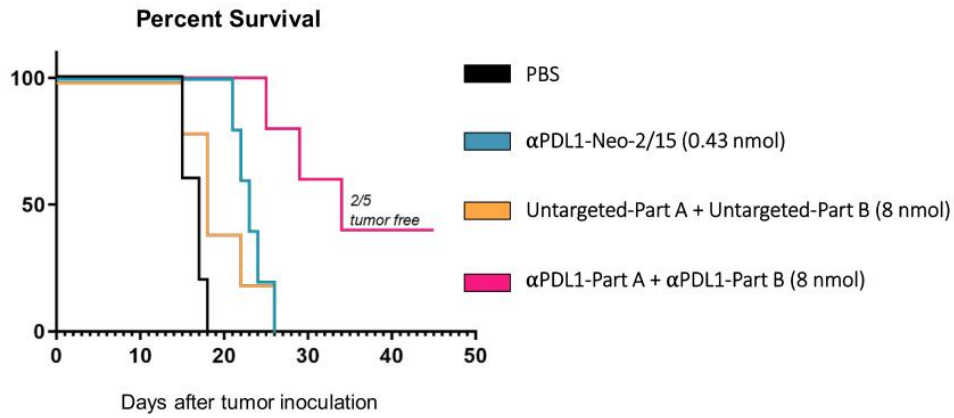
Some cytokine families have complex structures

# De Novo Split Technology: Conditionally Active IL-2 Mimetic



Quijano-Rubio et. al., AACR Virtual Annual Meeting II, Abstract #1075, Jun 2020

# Targeted Split Neo-2/15 Increases Therapeutic Window

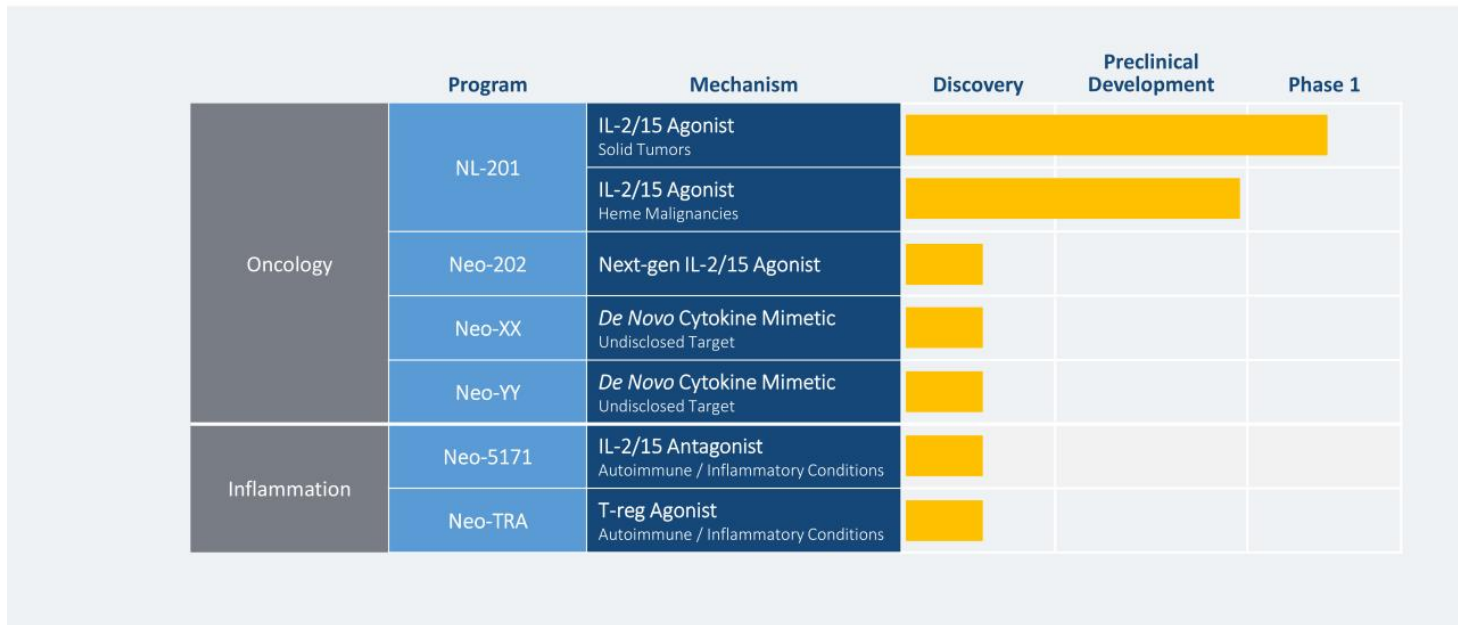


- C57BL/6J mice bearing B16 PDL1Hi melanoma cells in flank
- All groups were co-treated biweekly with Ta99 mAb (150 $\mu$ g/mice)
- Targeted Neo-2/15 variants and Part-A fusions administered i.p.; Part-B fusions administered s.c. opposite flank of tumor

Quijano-Rubio et. al., AACR Virtual Annual Meeting II, Abstract #1075, Jun 2020



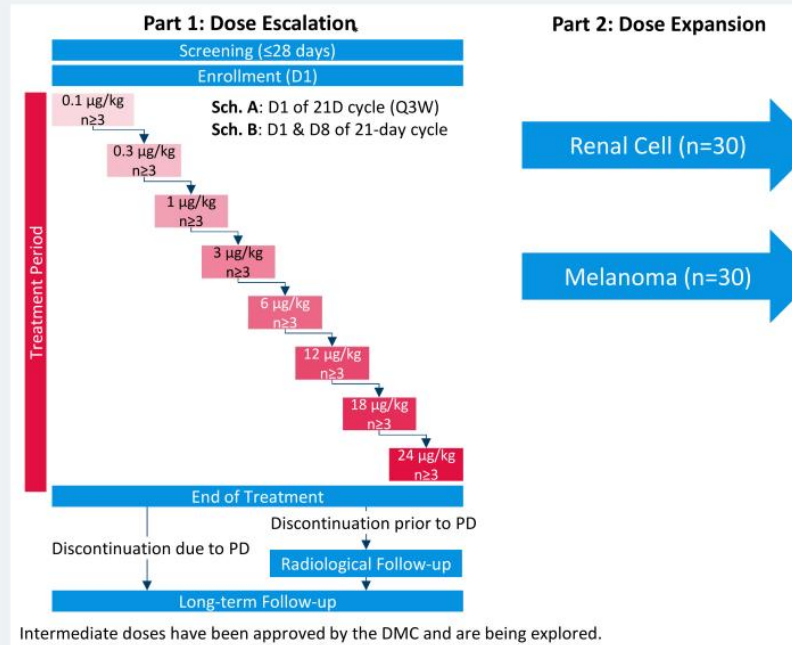
# Pipeline



NL-201 is believed to be the 1<sup>st</sup> *de novo* protein in clinic

# NL-201 Phase 1 Monotherapy Trial in Patients with Solid Tumors

- IV, monotherapy in patients with relapsed or refractory solid tumors
- Part 1: Identify optimal dose and schedule; assess safety, PK, PD, and antitumor activity
- Part 2: Indication-specific expansion cohorts, including renal cell carcinoma and melanoma
- Continuing to dose escalate; interim dose escalation data expected in 2023





## NL-201: Broad Opportunity in Cancer

- Solid tumor monotherapy trial ongoing
- Combination dosing with pembrolizumab began May 2022
- Heme trial initiation pending outcome of safety data in dose escalation in solid tumors
- Consider future opportunities to combine with monoclonal antibodies, cellular therapies and other standard-of-care agents
- Potential advantages of NL-201 local administration presented at SITC 2021

# NL-201 Turns 'Cold' Tumors 'Hot'

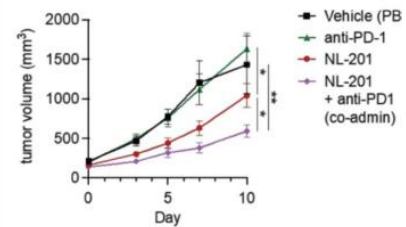
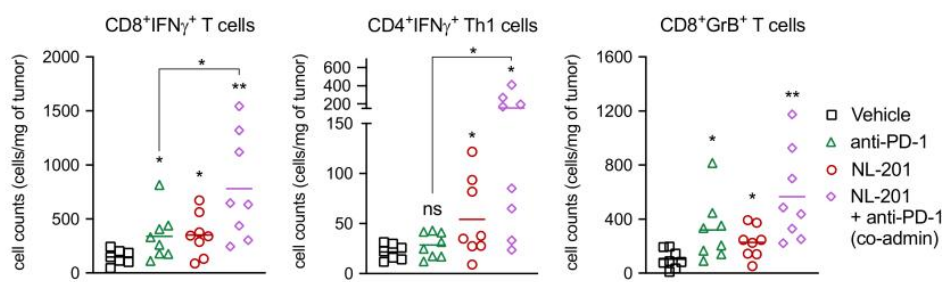
*Augments inflammatory milieu in preclinical B16 melanoma model*

## TCRβ Sequencing Summary

Mean (range)	Total T cells	Unique T cells	Simpson Clonality
Vehicle (n=5)	1,406 (358-2,708)	445 (196-807)	0.194 (0.106-0.411)
Anti-PD-1 (n=5)	2,456 (987-4,713)	464 (314-775)	0.34 (0.138-0.57)
NL-201 (n=5)	2,664 (1,578-3,816)	869 (611-1,064)	0.206 (0.11-0.292)
NL-201 plus anti-PD-1 (co-admin) (n=5)	2,865 (1,504-3,456)	1,042 (536-1,486)	0.128 (0.073-0.165)

## NL-201

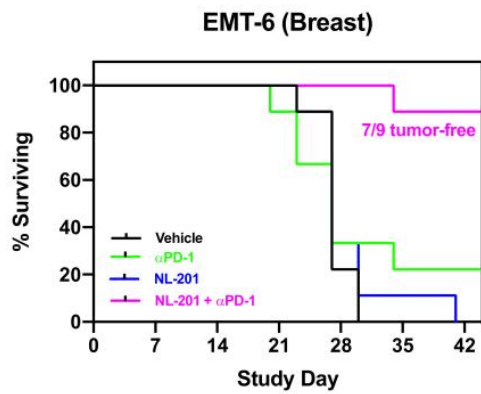
- increases T-cell diversity in the tumor microenvironment
- augments IFN $\gamma$  and granzyme expression in T-cells
- synergizes with anti-PD1 to inhibit tumor growth



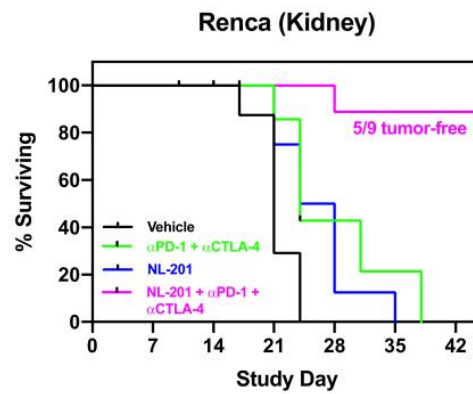
Mortales et. al, SITC 2021, Abstract #716, Nov 2021

# NL-201 Enhances Activity of Checkpoint Inhibitors in Preclinical Models

## Combination with NL-201 in CPI-resistant syngeneic tumors



$p=0.0029$ :  $\alpha$ PD-1 vs NL-201 +  $\alpha$ PD-1  
 $p<0.0001$ : NL-201 vs NL-201 +  $\alpha$ PD-1



$p=0.0001$ :  $\alpha$ PD-1 +  $\alpha$ CTLA-4 vs NL-201 +  $\alpha$ PD-1 +  $\alpha$ CTLA-4  
 $p=0.0006$ : NL-201 vs NL-201 +  $\alpha$ PD-1 +  $\alpha$ CTLA-4

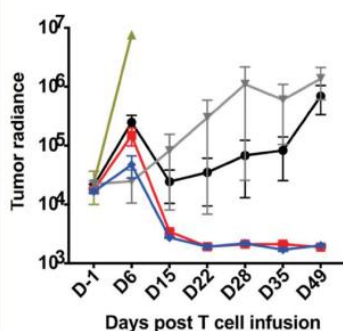
NL-201: 90 $\mu$ g/kg QWx2  
 $\alpha$ PD-1: 10mg/kg BiWx6  
 $\alpha$ CTLA-4: 10gm/kg BiWxt

Treatment began when tumors reached  $\sim 90\text{mm}^3$

# Promising NL-201 Preclinical Combinations In Vivo

## Enhanced antitumor activity with CAR-T cells and antibodies

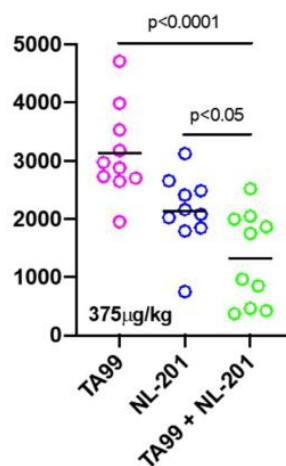
### RAJI Lymphoma Model



- NL-201 combined with a subcurative dose of CAR-T cells achieve deep tumor control and 100% survival
- NL-201 enhances intratumoral CD8:Treg ratios (~1000x vs. ~50x for IL-2)

Leung et. al, AACR Annual Meeting II, Abstract #2222, June 2020

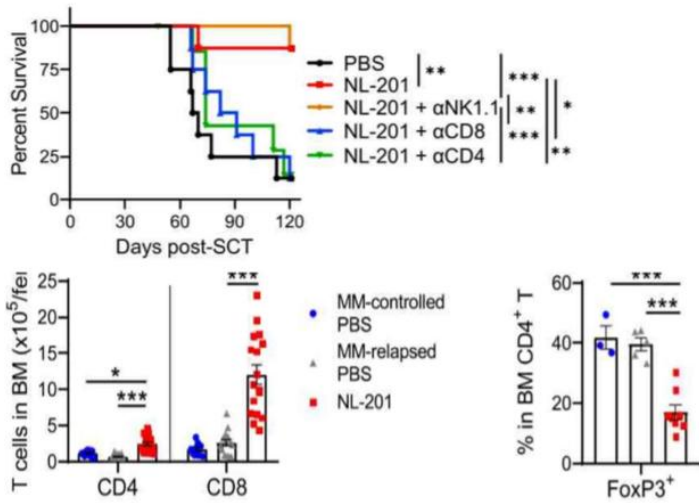
### B16 Melanoma Model



- NL-201 + TA99 (mAb) significantly improve tumor growth inhibition when combined

Walkey et. al, SITC 2020, Abstract #576, November 2020

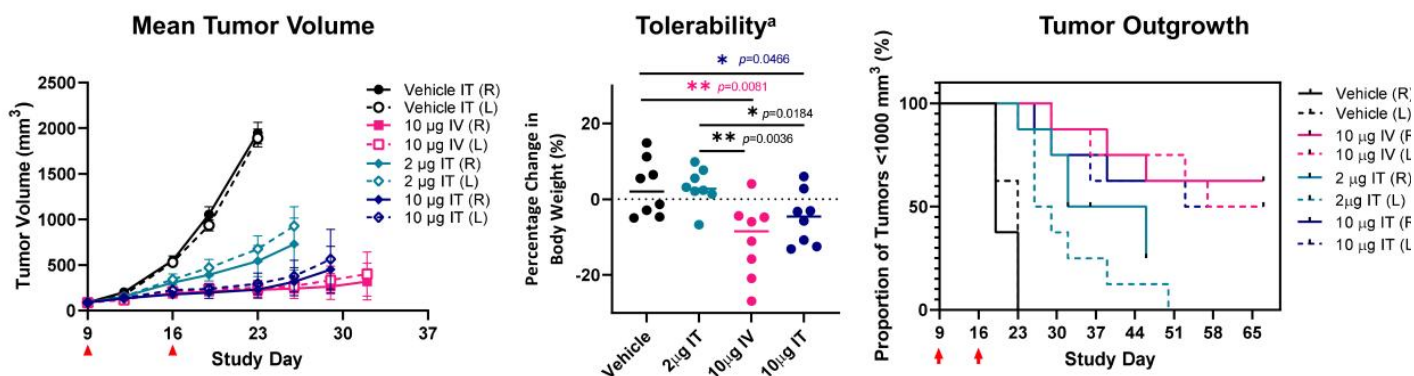
# NL-201 in Hematologic Malignancies: Preclinical Data



- NL-201 delays relapse in murine myeloma model following autologous stem cell transplant
- NL-201 induces expansion of cytotoxic CD8 T-cells and a decrease in T-regulatory CD4 cells in the bone marrow
- NL-201 treated mice had an increase in bone marrow T-cells expressing granzyme and a decrease in the T-cell exhaustion phenotype
- Planning to initiate Phase 1 trial for NL-201 in patients with hematologic malignancies based on dosing and safety data expected from solid tumor trial

Minnie et al, American Society of Hematology 63rd Annual Meeting. Abstract 1609. December 2021

# Intratumoral NL-201: Local and Distant Antitumor Control with Improved Tolerability



- CT26 syngeneic tumor model with bilateral tumor implants
- IT (R only) or IV NL-201 administered qWx2
- 10 mcg IV exceeded 20% weight loss in some mice

Tatalick et al, SITC 2021, Abstract #898, November 2021



# Focusing Efforts to Preserve Cash Runway

## Financial Highlights

- \$116.5 million cash, cash equivalents, and short-term investments as of June 30, 2022
- Cash and cash equivalents expected to fund operations through 2023
- 42.6M common shares outstanding and 12.7M pre-funded warrants<sup>1</sup>

## Cash Runway Focus

- Goal to ensure adequate runway to support achievement of NL-201 clinical milestones through 2023
- Focused operating plan around core value driving activities
- Reduced personnel growth to limit expenses

1. Warrants to purchase common shares 1:1 with an exercise price of \$0.000001 as of June 30, 2022.



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Designing for life.

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